

in their entireties. Applicants claim the benefits of these Applications under 35 U.S.C. §120.-

Please replace the last paragraph on Page 5 with:

- - The recognition factor is now known to comprise several proteinaceous substituents, in the instance of IFN $\alpha$  and IFN $\gamma$ . Particularly, three proteins derived from the factor ISGF-3 have been successfully sequenced and their sequences are set forth in FIGURE 1 (SEQ ID NOS:1, 2), FIGURE 2 (SEQ ID NOS:3, 4) and FIGURE 3 (SEQ. ID NOS.5, 6) herein. Additionally, a murine gene encoding the 91 kD protein (*i.e.*, the murine homologue of the human protein having an amino acid sequence of SEQ ID NO:4) has been identified and sequenced. The nucleotide sequence (SEQ ID NO:7) and deduced amino acid sequence (SEQ ID NO:8) are shown in FIGURE 13A-13C. - -

Please replace the second full paragraph of Page 7, beginning on line 9 with:

- - In a specific example, the receptor recognition factor represented by SEQ ID NO:4 possesses the added capability of acting as a transcription factor and, in particular, as a DNA binding protein in response to interferon- $\gamma$  stimulation. This discovery presages an expanded role for the proteins in question, and other proteins and like factors that have heretofore been characterized as receptor recognition factors. It is therefore apparent that a single factor may indeed provide the nexus between the liganded receptor at the cell surface and direct participation in DNA transcriptional activity in the nucleus. This pleiotypic factor has the following characteristics:

- a) It interacts with an interferon- $\gamma$ -bound receptor kinase complex;
- b) It is a tyrosine kinase substrate; and
- c) When phosphorylated, it serves as a DNA binding protein. - -

Please replace the bridging paragraph between Pages 8 and 9, beginning on line 29 of Page 8 with:

- - The present invention also relates to a recombinant DNA molecule or cloned gene, or a degenerate variant thereof, which encodes a receptor recognition factor, or a fragment

thereof, that possesses a molecular weight of about 113 kD and an amino acid sequence set forth in FIGURE 1 (SEQ ID NO:2); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding the 113 kD receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 1 (SEQ ID NO:1). In another embodiment, the receptor recognition factor has a molecular weight of about 91 kD and the amino acid sequence set forth in FIGURE 2 (SEQ ID NO:4) or FIGURE 13 (SEQ ID NO:8); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding the 91 kD receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 2 (SEQ ID NO:3) or FIGURE 13 (SEQ ID NO:8). In yet a further embodiment, the receptor recognition factor has a molecular weight of about 84 kD and the amino acid sequence set forth in FIGURE 3 (SEQ ID NO:6); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding the 84 kD receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 3 (SEQ ID NO:5). In yet another embodiment, the receptor recognition factor has an amino acid sequence set forth in FIGURE 14 (SEQ ID NO:10); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding such receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 14 (SEQ ID NO:9). In still another embodiment, the receptor recognition factor has an amino acid sequence set forth in FIGURE 15 (SEQ ID NO:12); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding such receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 15 (SEQ ID NO:11). - -

Please replace the fifth paragraph of Page 17, beginning on line 23 with:

- - FIGURE 1A-1E depicts the full receptor recognition factor nucleic acid sequence and the deduced amino acid sequence derived for the ISGF-3 $\alpha$  gene defining the 113 kD protein. The nucleotides are numbered from 1 to 2553 (SEQ ID NO:1), and the amino acids are numbered from 1 to 851 (SEQ ID NO:2). - -

Please replace the sixth paragraph of Page 17, beginning on line 28 with:

- - FIGURE 2A-2D depicts the full receptor recognition factor nucleic acid sequence and the deduced amino acid sequence derived for the ISGF-3 $\alpha$  gene defining the 91 kD protein. The nucleotides are numbered from 1 to 3943 (SEQ ID NO:3), and the amino acids are numbered from 1 to 750 (SEQ ID NO:4). - -

Please replace the first paragraph of Page 18, beginning on line 1 with:

- - FIGURE 3A-3C depicts the full receptor recognition factor nucleic acid sequence and the deduced amino acid sequence derived for the ISGF-3 $\alpha$  gene defining the 84 kD protein. The nucleotides are numbered from 1 to 2166 (SEQ ID NO:5), and the amino acids are numbered from 1 to 712 (SEQ ID NO:6). - -

Please replace the third paragraph of Page 18, beginning on line 19 with:

- - FIGURE 5a-5b generally presents the results of Northern Blot analysis for the 91/84 kD peptides. Figure 5a presents restriction maps for cDNA clones E4 (top map) and E3 (bottom map) showing DNA fragments that were radiolabeled as probes (probes A-D). Figure 5b comprises Northern blots of cytoplasmic HeLa RNA hybridized with the indicated probes. The 4.4 and 3.1 KB species as well as the 28S and 18S rRNA bands are indicated. -

Please replace the first full paragraph of Page 19, beginning on line 4 with:

- - FIGURE 7a-7e presents the results of Western blot and antibody shift analyses.

a) Highly purified ISGF-3, fractionated on a 7.0% SDS polyacrylamide gel, was probed with antibodies a42 (amino acids 597-703); a55 (amino acids 2-59); and a57 (amino acids 705-739) in a Western blot analysis. The silver stained part of the gel (lanes a, b, and c) illustrates the location of the ISGF-3 component proteins and the purity of the material used in Western blot: Lane a) Silver stain of protein sample used in all the Western blot experiments (immune and preimmune). Lane b) Material of equal purity to that shown in Fig. 4, for clearer identification of the ISGF-3 proteins. Lane c) Size protein markers indicated.

b) Antibody interference of the ISGF-3 shift complex; Lane a) The complete ISGF-3 and the free ISGF-3 $\gamma$  component shift with partially purified ISGF-3 are marked; Lane b) Competition with a 100 fold excess of cold ISRE oligonucleotide. Lane c) Shift complex after the addition of 1 ml of preimmune serum to a 12.5  $\mu$ l shift reaction. Lanes d and e) - Shift complex after the addition of 1  $\mu$ l of a 1:10 dilution or 1 ml of undiluted a42 antiserum to a 12.5  $\mu$ l shift reaction. - -

Please replace the first full paragraph of Page 23, beginning on line 4 with:

- -FIGURE 13 depicts (A) the deduced amino acid sequence (SEQ ID NO:8) of and (B- C) the DNA sequence (SEQ ID NO:7) encoding the murine 91 kD intracellular receptor recognition factor. - -

Please replace the second full paragraph of Page 23, beginning on line 8 with:

- - FIGURE 14 depicts (A) the deduced amino acid sequence (SEQ ID NO:10) of and (B-D) the DNA sequence (SEQ ID NO:9) encoding the 13sf1 intracellular receptor recognition factor. - -

Please replace the third full paragraph of Page 23, beginning on line 12 with:

- - FIGURE 15 depicts (A) the deduced amino acid sequence (SEQ ID NO:12) of and (B-E) the DNA sequence (SEQ ID NO:11) encoding the 19sf6 intracellular receptor recognition factor. - -

Please replace the bridging paragraph between Pages 37 and 38, beginning on line 23 of Page 37 with:

- - As stated above, the present invention also relates to a recombinant DNA molecule or cloned gene, or a degenerate variant thereof, which encodes a receptor recognition factor, or a fragment thereof, that possesses a molecular weight of about 113 kD and an amino acid sequence set forth in FIGURE 1 (SEQ ID NO:2); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding the 113 kD receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown

in FIGURE 1 (SEQ ID NO:1). In another embodiment, the receptor recognition factor has a molecular weight of about 91 kD and the amino acid sequence set forth in FIGURE 2 (SEQ ID NO:4) or FIGURE 13 (SEQ ID NO:8); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding the 91 kD receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 2 (SEQ ID NO:3) or FIGURE 13 (SEQ ID NO:8). In yet a further embodiment, the receptor recognition factor has a molecular weight of about 84 kD and the amino acid sequence set forth in FIGURE 3 (SEQ ID NO:6); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding the 84 kD receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 3 (SEQ ID NO:5). In yet another embodiment, the receptor recognition factor has an amino acid sequence set forth in FIGURE 14 (SEQ ID NO:10); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding such receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 14 (SEQ ID NO:9). In still another embodiment, the receptor recognition factor has an amino acid sequence set forth in FIGURE 15 (SEQ ID NO:12); preferably a nucleic acid molecule, in particular a recombinant DNA molecule or cloned gene, encoding such receptor recognition factor has a nucleotide sequence or is complementary to a DNA sequence shown in FIGURE 15 (SEQ ID NO:11). - -

Please replace the bridging paragraph between Pages 69 and 70, beginning on line 30 of Page 69 with:

- - A fragment of the gene encoding the human 91 kD protein was used to screen a murine thymus and spleen cDNA library for homologous proteins. The screening assay yielded a highly homologous gene encoding a murine polypeptide that is greater than 95% homologous to the human 91 kD protein. The nucleic acid and deduced amino acid sequence of the murine 91 kD protein are shown in Figure13A-13C, and SEQ ID NO:7 (nucleotide sequence) and SEQ ID NO:8 (amino acid sequence). - -